UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,095	04/07/2005	Henry M Krause	1889-00900	5757

23505 7590 08/08/2006

CONLEY ROSE, P.C.
P. O. BOX 3267
HOUSTON, TX 77253-3267

EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/531,095	KRAUSE ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-9,18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-17 and 20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Pending Claims

Applicant's election without traverse of claims 10-17 and 20-22 in the reply filed on June 26, 2006 is acknowledged. Claims 1-9 and 18-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Accordingly, claims 1-22 are pending and claims 10-17 as well as 20-22 are under examination.

Specification

The disclosure is objected to because of the following informalities: Page 17 of the instant specification contains a large blank area. It is unclear whether this area except for 4 lines of the disclosure is left blank intentionally or some content of the disclosure is missing.

Appropriate correction is required.

Claim Objections

Claims 14-15 and 20 are objected to for containing non-elected subject matter. Appropriate correction is required.

Claims 14-15 and 20 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 10, 12, 15-17, and 20-22 are rejected under 35 U.S.C. 102(a) as being anticipated by Srisawat et al. (*Methods,* 26:15-161, 2002).

Claims 10, 12, 15-17, and 20-22 are directed to an RNA fusion molecule comprising a target RNA sequence and at least two different RNA tags, wherein at least one RNA tag interacts with a ligand in a reversible fashion and the RNA tags are streptavidin binding sequence (S1) and a sephadex binding sequence (D8), a DNA construct encoding the RNA fusion molecule, a vector comprising the DNA construct, and a host cell comprising the vector.

Given the broadest reasonable interpretation of claim 10 consistent with the instant specification, "at least one RNA tag interacts with a ligand in a reversible fashion" (lines 3-4) will be construed to mean that ribonucleoprotein complexes, formed by interaction between the RNA tag and its ligand, can be eluted intact from the first ligand matrix and bound to the second matrix in light of the disclosure (page 11).

Srisawat et al. teach a fusion RNA molecule comprising the yeast RPR1 gene as a target sequence attached to two different RNA tags, S1 and D8, which is inserted into a low-copy plasmid, wherein the plasmid containing the fusion RNA molecule is then inserted into a yeast cell. They teach that S1 has high affinity for biotin whereas D8 has high affinity for dextran. They teach that the isolation of RPR1 RNA from yeast lysates containing the S1- plus D8-tagged

RPR1 can be achieved via affinity isolation using the S1 and D8 agarose matrix followed by elution with biotin/dextran or via two sequential purification steps to attain high levels of purity. Thus, all the limitations of claims 10, 12, 15-17, and 20-22 are met by Srisawat et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-12, 14-17, and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srisawat et al. as applied to claims 10, 12, 15-17, and 20-22 above for §102 rejections, and further in view of Rigaut et al. (*Nature Biotechnology,* 17: 1030-1032, 1999).

Claims 10-12, 14-17, and 20-22 are drawn to an RNA fusion molecule comprising a target RNA sequence and at least two different RNA tags, wherein at least one RNA tag interacts with a ligand in a reversible fashion and at least one RNA tag is repeated, and the RNA fusion molecule further comprising at least one insulator sequence, a DNA construct encoding the RNA fusion molecule, a vector comprising the DNA construct, and a host cell comprising the vector.

Given the broadest reasonable interpretation of the term, "insulator" of claim 14 consistent with the instant specification, "insulator' will be interpreted as synonymous with "spacer" based on the instant specification disclosing that "insulator elements may also be called spacers" (page 15).

As described above, Srisawat et al. teach an RNA fusion molecule comprising an RNA target sequence and S1 and D8 RNA tags (claims 10 and 12), a plasmid vector comprising the RNA fusion molecule (claims 15-16), and a yeast host cell comprising the plasmid vector (claim 17). They do not teach an RNA fusion molecule wherein at least one RNA tag is repeated (claim 11) or the fusion molecule further comprising at least one insulator sequence (claim 14). They teach that the RNA tags can be used to rapidly and specifically isolate a particular precursor or product form of RNA of interest from RNPs or characterization of RNPs containing lethal mutations (page 161).

However, at the time the instantly claimed invention was made, it was routine to make a fusion molecule with repeated tags and spacers. Rigaut et al. teach a host cell comprising a DNA cassette encoding a tandem affinity purification (TAP) tag that is fused to a target protein, wherein the TAP tag comprises calmodulin binding peptide and two repeated IgG binding domain of protein A of *Staphylococcus aureaus* (ProtA) associated with a TEV cleavage site. They teach that the TEV cleavage site is flanked by insulators (synonymous with spacers) at each end. They teach that the fusion protein and associated components are first eluted by affinity selection on an IgG matrix and addition of TEV protease. This elution is then bound to calmodulin-coated beads in the presence of calcium, indicating that the interaction between the TAP tag and ligand is reversible. They also teach that the TAP strategy can be used to purify a specific complex and is not limited to identifying protein-protein interactions.

It would have been obvious to one of ordinary skill in the art at the time of the instantly claimed invention to make an RNA fusion molecule of Srisawat et al. by inserting two repeated RNA tags and spacers as taught by Rigaut et al. One of ordinary skill in the art would have been motivated to combine the teachings of the prior art with a reasonable expectation of success

because the structure of the TAP tag fusion construct containing two repeated IgG binding domains and two spacers of Rigaut et al. results in a successful identification of new proteins that are associated with the target protein. Because Srisawat et al. have already taught that the isolation of a tagged RNP via RNA tags can be used to rapidly and specifically isolate a particular precursor or product form of RNA of interest from the RNA-protein complex and because the purification system of Rigaut et al. comprising two insulators and repeated tags was successfully used to purify a specific complex, the skilled artisan would have been sufficiently motivated to make an RNA fusion molecule of Srisawat et al. by adding additional components such as insulators and repeated RNA tag sequences as taught by Rigaut et al. Accordingly, the instantly claimed invention taken as a whole is *prima facie* obvious.

Claims 10, 12-13, 15-17, and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srisawat et al. as applied to claims 10, 12, 15-17, and 20-22 above for §102 rejections, and further in view of Johansson et al. (*PNAS,* 95:9244-9249, 1998).

Claims 10, 12-13, 15-17, and 20-22 are drawn to an RNA fusion molecule comprising a target RNA sequence and at least two different RNA tags, wherein at least one RNA tag interacts with a ligand in a reversible fashion and the RNA tags comprise at least one streptavidin binding sequence (S1) and at least one MS2 coat protein binding sequence, a DNA construct encoding the RNA fusion molecule, a vector comprising the DNA construct, and a host cell comprising the vector.

Srisawat et al. teach a fusion molecule comprising a target sequence and two different tags (S1 and D8) that interact with a ligand in a reversible fashion. They do not teach a fusion

molecule comprising S1 and MS2 coat protein binding sequence (claim 13) nor a DNA construct/vector/host cell comprising S1 and MS2.

However, at the time of the instantly claimed invention, it was routine in the art to use MS2 coat protein sequence as an RNA tag sequence that forms an RNA-protein complex . Johansson et al. teach that MS2 coat protein specifically binds to RNA hairpins and this protein-RNA interaction has been extensively studied as a model for the rapidly expanding class of proteins that bind RNA hairpins.

It would have been obvious to one of ordinary skill in the art at the time of the instantly claimed invention to make an RNA fusion molecule having at least one MS2 coat protein binding sequence of Johansson et al. by modifying the teachings of Srisawat et al., which teach an RNA fusion molecule comprising an RNA target sequence and S1 and D8 RNA tags. Thus, one of ordinary skill in the art would have been sufficiently motivated to substitute the D8 tag for MS2 coat protein binding sequence tag so as to make an RNA fusion molecule/isolated DNA construct/vector/host cell having S1 and MS2 coat protein tags, instead of S1 and D8 of Srisawat et al., because Johansson et al. teach that MS2 coat protein has been utilized as a binding assay component for studies involving protein-RNA interaction. Further, it is an art-recognized practice to replace one type of tag sequence in a DNA construct with another type of tag sequence when the two tag sequences are functionally equivalent. Since both MS2 and D8 function as RNA tag sequences that can be utilized in a riboprotein purification method as taught by Srisawat et al. and Johansson et al, the skilled artisan would have had a reasonable expectation of success in making the RNA fusion molecule comprising S1 and MS2 coat protein tags. Accordingly, the instantly claimed invention taken as a whole is *prima facie* obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

Dana Shin
August 3, 2006

TC1600

JANE ZARA, PH.D.
PRIMARY EXAMINER